Obesity Management Strategies: Endoscopic Bariatric Therapy

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Disclosure

• The following are my disclosures. Potential conflicts of interest have been resolved.

  □ No disclosures
Obesity in America

- 36.5% of US population has obesity
- Higher prevalence among African American (48.1%) and Hispanic (42.5%) populations, and people with lower income
- Multiple associated comorbidities include heart disease, stroke, diabetes, certain cancers
- Estimated annual cost $147 billion (average healthcare costs $1400/year higher for patients with obesity vs. those without)
Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016

*Sample size <50 or the relative standard error (dividing the standard error by the prevalence) ≥ 30%.
Obesity management

- Lifestyle modification
- Medications
- Surgery
- Endoscopy
Primary endoscopic therapy

- American Society for Gastrointestinal Endoscopy (ASGE) position statement supports use of endoscopic bariatric therapy (EBT) in conjunction with a multidisciplinary weight loss program
- Consider EBT in patients who:
  - Have failed weight loss or maintenance with lifestyle intervention alone
  - Meet BMI criteria for particular treatment modalities
  - Have medical conditions that require weight loss of additional therapy (e.g. bridge therapy to weight loss surgery)
- Current approved and investigational devices include space-occupying devices, tissue apposition devices, and nutrient-diverting devices

Garren-Edwards Gastric Bubble

Garren-Edwards Gastric Bubble

- First described in 1982 and FDA approved in 1985
- Air filled balloon, placed endoscopically
- Pulled from market in 1992 due to adverse events including gastric mucosa injury, small bowel obstruction following deflation and migration, poor efficacy
- Likely reasons for failure:
  - Material: polyurethane, deflated too easily
  - Shape: cylindrical, with edges leading to ulcers
  - Size: 220 mL volume, 400 mL minimum to decrease food intake
- After this experience no intragastric balloon was approved by the FDA until 2015

Fluid-filled single balloon: Orbera

- Spherical silicone balloon
- Placed endoscopically, filled with saline (often containing methylene blue)
- Filled to 400-700 mL
- Remains in place for 6 months, removed endoscopically
- Introduced 1991, previously called Bioenteric Intragastric Balloon (BIB)
- Has been evaluated in multiple studies, available elsewhere since 1990s
Orbera adverse events

Orbera: weight loss kinetics

Orbera: durability of weight loss

Contraindications (FDA)

- Prior GI or bariatric surgery
- Inflammatory disease of GI tract e.g. esophagitis, ulcer disease, cancer, Crohn’s
- Potential upper GI bleeding conditions e.g. varices, telangectasias; or congenital anomalies e.g. atresias
- Large hiatal hernia > 5 cm or smaller with severe reflux symptoms
- Structural abnormality in esophagus or pharynx e.g. stricture or diverticulum
- Achalasia or other severe motility disorder
- Gastric mass
- Coagulopathy
- Cirrhosis or other serious comorbid condition
- Serious or uncontrolled psychiatric illness
- Alcohol or drug addiction
- Unwillingness to take PPI, stop NSAIDs, or participate in diet and behavior program
- Pregnancy or breast feeding
Fluid-filled dual balloon: ReShape

- Two silicone balloons connected by flexible shaft
- Placed endoscopically, each filled 375 or 450 mL saline + methylene blue
- Designed to prevent migration
- Removed endoscopically at 6 months

- FDA approved 2015
- Product has recently been discontinued

ReShape Medical, San Clemente, CA
Gas-filled swallowed balloon: Obalon

- Gelatin capsule with attached catheter, swallowed under fluoro
- Inflate with 250 mL nitrogen-mix gas
- Can swallow up to 3 balloons over 6 month course
- Removed endoscopically
- Per FDA, average weight loss 14.4 lbs or 6.6% total weight

A. Swallowable capsule containing balloon
B. Inflation device
C. Gas-filled balloon
D. Radiograph of three deployed balloons in vivo

Obalon Therapeutics, Carlsbad, CA.

Serious adverse events included:
- hospital admissions for nausea, vomiting, pain, or device removal (75%)
- 1 esophageal mucosal tear, 1 contained esophageal perforation, 1 bleeding gastric ulcer, 1 aspiration pneumonitis (ReShape)
- 1 gastric outlet obstruction, 1 gastric perforation, 1 aspiration pneumonia, 2 esophageal tears, 1 laryngospasm, 1 infected balloon (Orbera)
- 1 bleeding gastric ulcer (Obalon)
Adverse event comparison

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>ReShape (%)</th>
<th>Orbera (%)</th>
<th>Obalon (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>86.7</td>
<td>86.8</td>
<td>17.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>61.0</td>
<td>75.6</td>
<td>56.0</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>54.5</td>
<td>57.5</td>
<td>72.6</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>35.2(^a)</td>
<td>0</td>
<td>0.9</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>17.8</td>
<td>21.3</td>
<td>16.9(^c)</td>
</tr>
<tr>
<td>Eructation</td>
<td>16.7</td>
<td>24.4</td>
<td>9.2</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>13.3</td>
<td>6.3</td>
<td>0</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>11.0</td>
<td>17.5</td>
<td>14.6</td>
</tr>
<tr>
<td>Erosive gastritis</td>
<td>9.1</td>
<td>0.6</td>
<td>7.1(^b)</td>
</tr>
<tr>
<td>GERD</td>
<td>6.8</td>
<td>30.0</td>
<td>(see dyspepsia)</td>
</tr>
<tr>
<td>Erosive esophagitis</td>
<td>0.4</td>
<td>0.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.3</td>
<td>0</td>
<td>2.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3.0</td>
<td>13.1</td>
<td>8.3</td>
</tr>
</tbody>
</table>

GERD, gastroesophageal reflux disease; SAE, serious adverse event.

\(^a\)After design modification of the distal tip of the ReShape Balloon, the ulcer rate decreased to 10%.

\(^b\)Composite of erythema, erosion, inflammation, or polyp.

\(^c\)Composite of dyspepsia and GERD.

Endoscopic sleeve gastroplasty (ESG)

- Endoscopic suturing device used to create a gastric sleeve
- Uses FDA approved device. 98 min average procedure time.
- Fits on end of double channel endoscope.
- Curved needle driver produces full-thickness sutures

A. Suturing pattern used
B. Endoscopic suturing device (Apollo Overstitch)
C. Depiction of procedure

ESG Weight loss kinetics

ESG effect on obesity-related comorbidities

ESG multicenter study

- 3 center study in US and Spain
- 248 patients
- 15.7% TWL at 6 months, 18.6% at 24 months
- Five serious adverse events: inflammatory fluid collections (adjacent to fundus), self-limited hemorrhage, pulmonary embolism, pneumothorax; none required surgery

Aspiration therapy

- Large silicone gastrostomy tube (A-tube) placed endoscopically using standard pull PEG technique
- Connected to Aspire Assist device
- Patient siphons off a third of ingested meal
- Works by diversion of calories and change in behavior causing decreased food intake (chewing longer, drinking more water)
Aspire efficacy

Average weight loss 14.2%, with 59% of patients reaching 10% TWL

**Table 2.** Adverse events occurring in 5% or more of participants and serious adverse events in the AspireAssist group (N=111), and time period in which the event occurred (i) <7 days (perioperative) and (ii) >7 days (postoperative) of A-tube placement

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>No. of participants (%)</th>
<th>No. of participants, perioperative</th>
<th>No. of participants, postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peristomal granulation tissue</td>
<td>45 (40.5%)</td>
<td>0</td>
<td>45</td>
</tr>
<tr>
<td>Abdominal pain within 4 weeks after A-tube placement*</td>
<td>42 (37.8%)</td>
<td>41</td>
<td>1</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>19 (17.1%)</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Peristomal irritation</td>
<td>19 (17.1%)</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Intermittent abdominal discomfort</td>
<td>18 (16.2%)</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Possible or definite peristomal bacterial infection</td>
<td>15 (13.5%)</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Abdominal pain 4 weeks or more after A-tube placement*</td>
<td>9 (8.1%)</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Dyspepsia (acid reflux, heartburn, hiccups, belching)</td>
<td>7 (6.3%)</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Peristomal inflammation</td>
<td>6 (5.4%)</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

**Serious adverse events**

- Severe abdominal pain 1 (0.9%) 1
- Peritonitis 1 (0.9%) 1
- Pre-pyloric ulcer 1 (0.9%) 1
- A-tube replacement because of Skin-Port malfunction 1 (0.9%) 1

*Defined as abdominal pain not relieved with standard oral analgesic therapy.
Why endoscopic therapy?

- More weight loss compared with lifestyle therapy and medications
- Less weight loss than surgery, but fewer complications and lower cost
- Only 1-2% of patients eligible for bariatric surgery undergo an operation
- Endoscopy may help fill this treatment gap
- Rapid advancement of this field continues to produce new approaches
Approach to therapy

• Start with lifestyle modification; important to any regimen
• Triage patients to appropriate therapy (medical, endoscopic, surgical)
• Screen for physical and psychological comorbidities; careful patient selection is important
• Program should couple endoscopic therapy with dietary and behavioral counseling
Conclusions

- Multiple EBTs are currently being used in the US for primary obesity treatment, and several studies have shown benefit with large randomized sham controlled and non-sham controlled designs.
- Multiple EBTs are under review by the FDA or are in the investigational phase for FDA approval.
- EBT should be used in conjunction with at least moderate intensity lifestyle therapy as part of a comprehensive long-term weight management program for maximal benefit.
Thank you!